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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FETTEROLF, BRANDON J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/707,994	ALBERTO ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-17 and 19-21* is/are rejected.

7)☒ Claim(s) *10 and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1-21 are currently pending and under consideration.

Information Disclosure Statement

The Information Disclosure Statement filed on 4/29/2004 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS is attached hereto.

Claim Objections

Claims 16 and 17 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, it is unclear how claim 16's recitation of the intercalating agent being an aromatic molecule with an intercalative binding affinity for double stranded DNA further limits claim15.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 11, 17 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 5 and 17, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claims 11 and 19, the reference to any one of the structures as shown in Figure 1 renders the claim indefinite because it is unclear whether the "pyridine" is part of the intercalator or whether the "pyridine" has been added to the intercalator for functionalization. See MPEP § 2173.05(d).

Claims 1-4, 6-7, 9, 11-13, 15-16 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are inclusive of a genus of compounds referred to as an "intercalating moiety". Therefore, the claims encompass a genus of compounds defined solely by their principal biological property, which is simply a wish to know the identity of any material with that biological property. However, the written description in this case only sets forth intercalating moieties selected from the group consisting of acridine, porphyrin, ellipticine, phenantroline, carbazole, benzimidazole, daunorubicine, epirubicine, mixoxantrone and the structure shown in figure 2.

The Written Description Guidelines for examination of patent applications indicates, "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical characteristics and/or other chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show applicant was in possession of the claimed genus." (Federal register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3) and (see MPEP 2164).

The specification teaches (page 4, paragraph 0011) that specific intercalating moieties of the invention include, but are not limited to, aromatic molecules with an intercalative binding affinity for double stranded DNA. The specification further teaches (page 5, paragraph 0011) that examples of such aromatic compounds are compounds containing, for example, acridine, porphyrin, ellipticine, phenantroline, carbazole, benximidazole or compound with known cytostatic activity (for example antibiotics from the class of tetracyclines (anthracyclines)) such as daunorubicine, epirubicine, or mixoxantrone. Moreover, the specification further provides a structural representation of an intercalating moiety shown in figure 2. Thus, while the specification reasonably conveys intercalating moieties selected from the group consisting of acridine, porphyrin, ellipticine, phenantroline, carbazole, benzimidazole, daunorubicine, epirubicine, mixoxantrone and the molecule of formula 1, as noted above, the claims encompass a genus of molecules defined solely by

its principal biological property, which is simply a wish to know the identity of any material with that biological property. Accordingly, there is insufficient written description encompassing an "intercalating moiety" because the relevant identifying characteristics of the genus such as structure or other physical and/or chemical characteristics of an "intercalating moiety" are not set forth in the specification as-filed. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of molecules that encompass the genus of intercalating moieties nor does it provide a description of structural features that are common to the genus. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of intercalating moieties, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only intercalating moieties selected from the group consisting of acridine, porphyrin, ellipticine, phenantroline, carbazole, benzimidazole, daunorubicine, epirubicine, mixoxantrone and the structure shown in figure 2, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 12-13, 15-17 and 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Toner et al. (W0 93/21957, 1993, IDS) as evidenced by Albert et al. (US 5,776,894, 1998).

Toner et al. teach a targeting radioactive immunoreagent comprising a metal radionuclide ion, a complexing agent which is a derivative of phenantroline and an immunoreactive group covalently bonded through a protein reactive group to the complexing agent (page 6, lines 1-10 and page 8, lines 9-13, structure A-IV). With regards to the immunoreactive group, the WO document teaches that the inmmunoreactive group includes, but is not limited to, antibodies such as B72.3, 9.2.27, D612, UJ13A, NRLU-10, 7E11c5, CC49, TNT, PR1A3, ING-1, B174 and B43 antibodies (page 122). With regards to the metal radionuclide ion, the WO document teaches that the radionuclide ion is ^{90}Y (page 122). In addition to the disclosure of a targeting radioactive immunoreagent, the WO document teaches a diagnostic composition and a therapeutic composition comprising the radioactive immunoreagent, as well as a method of diagnosing and treating a patient using said radioactive immunoreagent (page 122). Specifically, the WO document teaches that the radioactive immunoreagent are used for the diagnosis and treatment of a tumor, wherein the immunoreagent is an antibody specific for a tumor antigen (page 61, lines 21-31). Thus, while Toner et al. do not explicitly teach that ^{90}Y is a γ emitting nuclide, the claimed limitation does not appear to result in a manipulative difference when compared to the prior arts disclosure in because as evidenced by Albert et al.et al., γ emitting nuclides include, but are not limited to, ^{90}Y (column 11, lines 3-8).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 9 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Toner et al. (W0 93/21957, 1993, IDS) in view of Albert et al. (US 5,776,894, 1998).

Toner et al. teach, as applied to claims 1-8, 12-13, 15-17 and 20-21 above, a targeting radioactive immunoreagent comprising a metal radionuclide ion, a complexing agent which is a derivative of phenantroline and an immunoreactive group covalently bonded through a protein reactive group to the complexing agent (page 6, lines 1-10 and page 8, lines 9-13, structure A-IV).

With regards to the immunoreactive group, the WO document teaches that the inmmunoreactive group includes, but is not limited to, antibodies such as B72.3, 9.2.27, D612, UJ13A, NRLU-10, 7E11c5, CC49, TNT, PR1A3, ING-1, B174 and B43 antibodies (page 122). With regards to the metal radionuclide ion, the WO document teaches that the radionuclide ion is ^{90}Y (page 122). In addition to the disclosure of a targeting radioactive immunoreagent, the WO document teaches a diagnostic composition and a therapeutic composition comprising the radioactive immunoreagent, as well as a method of diagnosing and treating a patient using said radioactive immunoreagent (page 122). Specifically, the WO document teaches that the radioactive immunoreagent are used for the diagnosis and treatment of a tumor, wherein the immunoreagent is an antibody specific for a tumor antigen (page 61, lines 21-31).

Toner et al. do not explicitly teach that the radioactive metal is selected from the group consisting of Tc-99m, Re-186, Re-188 and Mn.

Albert et al. teach somatostatin peptides bearing at least one chelating group with a detectable element, wherein the detectable elements includes, but is not limited to, g-emitting radionuclides such as Tc-99 and Re-186 (abstract and column 11, lines 3-8). Moreover, Albert et al. teach that the somatostatin peptide bearing at least one chelating group with a detectable element are useful for the visualization and treatment of somatostatin receptor positive tumors (column 12, lines 26-35).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute 90Y as taught by Toner et al. for Tc-99 or Re-186 in view the Albert et al teachings that 90Y, Tc-99 and Re-186 are known γ and β emitters As such, one would have been motivated to do so because Albert et al. teach that 90Y, Tc-99 and Re-186 are each γ and β emitters useful for treatment and visualization of tumors. Thus, one of ordinary skill in the art would have a reasonable expectation that by substituting 90Y as taught by Toner et al. for Tc-99 or Re-186 in view the Albert et al, one would achieve a targeted radioactive immunoreagent for the treatment and diagnosis of a tumor.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 12-14, and 20-21 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,844,425.

Although the conflicting claims are not identical, they are not patentably distinct from each other because a species anticipates a genus.

The "species" compound comprising: (a) a biomolecule selected from somatostatin, neurotensin, bombesin-receptor binding molecules, antibodies, antennapedia peptide, and molecules binding to GPIIb/GPIIIa receptors; coupled to (b) an aromatic intercalating moiety with binding affinity for double-stranded DNA selected from acridine, porphyrin, ellipticine, phenantroline, carbazole, benzimidazole, and tetracycline compounds with cytostatic activity; which is complexed to (c) a .gamma.-emitting radioactive metal selected from Tc-99m, Re-186, Re-188, and Mn, wherein said compound is associated with one or more pharmaceutically acceptable excipients claimed in the conflicting patent appears to fall within the same scope as the genus of compounds comprising (a) a biomolecule selected from the group consisting of somatostatin, neurotensin, bombesin-receptor binding molecules, antibodies, penetratines.TM., and molecules binding to GPIIb/IIIa receptors; coupled to (b) an aromatic intercalating moiety with binding affinity for double-stranded DNA selected from the group consisting of acridine, porphyrin, ellipticine, phenantroline, carbazole, benzimidazole, and tetracycline compounds with cytostatic activity; which is complexed to (c) a .gamma.-emitting radioactive metal selected from Tc-99m, Re-186, Re-188 and Mn and a diagnostic and/or therapeutic composition comprising a tumor-seeking biomolecule; ii. an intercalating moiety

coupled to said tumor-seeking biomolecule; and iii. a metal compound complexed to said intercalating moiety claimed in the instant application being examined.

Conclusion

Tommasi et al. (Inorg. Chem. 1995; 34: 1514-1523), considered closest prior art for claims 10 and 18, teach the synthesis of pyrroloquinolinequinone analogs complexed with Iron, e.g., Fe. However, the Tommasi et al. do not teach or suggest the compound as shown in Figure 2. As such, claims 10 and 18 are objected to for being dependent from a rejected independent claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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